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cont

with a polypeptide capable of forming a complex with the moiety A [and] , said polypeptide including a moiety which can be detected when said complex is formed.

105. (Twice Amended) The method of claim 104 wherein the moiety A of said compound [comprises] is selected from the group consisting of biotin and iminobiotin.

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107. (Amended) The method of claim 104 wherein the moiety A is a hapten and said polypeptide is an antibody thereto.

108. (Amended) The method of claim 104 wherein the moiety A is a ligand.

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113. (Twice Amended) A method of detecting a double-stranded polynucleotide duplex which includes a compound in accordance with Claim [125] ¹⁴⁸ ~~145~~ which comprises contacting said polynucleotide duplex with a polypeptide capable of forming a complex therewith under suitable conditions as to form said complex, said polypeptide including a moiety which can be detected when said complex of said polynucleotide duplex and said polypeptide is formed, and detecting said complex.

114. (Amended) A method in accordance with claim 113 wherein the moiety A of said polynucleotide duplex [comprises] is selected from the group consisting of biotin and iminobiotin.

115. (Amended) A method in accordance with claim 113 wherein said polypeptide [comprises] is selected from the group consisting of avidin, streptavidin, and [IgG] anti-A immunoglobulin.

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118. (Amended) A method in accordance with claim 113 wherein the moiety included in said polypeptide which can be detected is [a] fluorescent [dye], electron dense [reagent], or is an enzyme capable of [depositing] an insoluble reaction product] reacting with a substrate to form a detectable reaction product.

126. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ wherein said target is a nucleic acid [sequence] derived from a living organism.

128. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ wherein said sample is suspected of containing an etiological agent and said target nucleic acid [sequence] is naturally associated with said etiological agent.

130. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ wherein said sample comprises a [bacterium] microorganism suspected of containing a target nucleic acid [sequence] which imparts resistance to an antibiotic and wherein said compound comprises a polynucleotide complementary to the [sequence] nucleic acid of said [bacterium] microorganism which confers resistance to said antibiotic.

In claim 131, delete the word "bacterium" and substitute the word --microorganism-- therefor.

In claim 132, delete the word "bacterium" and substitute the word --microorganism-- therefor.

In claim 133, delete the word "bacterium" and substitute the word --microorganism-- therefor.

134. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ wherein said sample is suspected of containing a target nucleic acid [sequence] associated with a genetic disorder and wherein said compound comprises a polynucleotide complementary to the [sequence] nucleic acid associated with said genetic disorder.

135. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ wherein said sample is suspected of containing a target nucleic acid [sequence] associated with thalassemia and wherein said compound comprises a polynucleotide complementary to the [sequence] nucleic acid which is absent in thalassemic subjects.

136. (Amended) The method of claim [125] ¹⁴⁸ ~~146~~ for chromosomal karyotyping which comprises contacting said sample

with a series of said compounds which are complementary to a series of known genetic [sequences] nucleic acids located on chromosomes.

137. (Amended) The method of claim [125] ¹⁴²~~146~~, wherein said sample is suspected of containing a target polynucleotide which includes a terminal polynucleotide [sequence] poly A and wherein said compound comprises a modified poly U nucleotide [sequence] in which at least one uracil moiety has been modified by [chemical addition at the 5' position of A] the attachment of the moiety A at the 5-position.

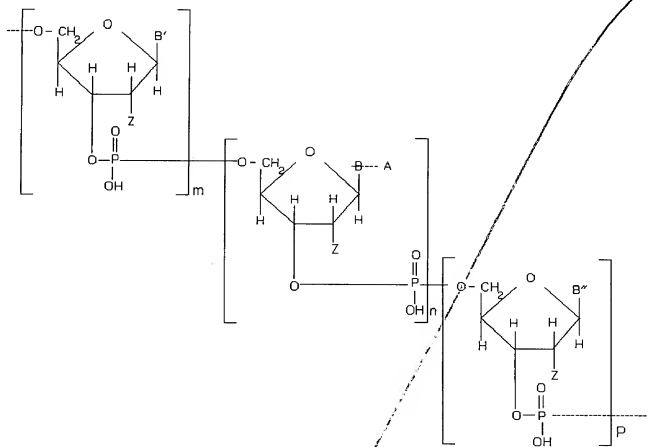
141. (Amended) The method of claim [140] ¹⁴⁹~~147~~, which comprises detecting malignant cells by detecting abnormal hormonal receptor sites associated therewith.

142. (Amended) The method of claim [125] ¹⁴⁸~~146~~, wherein said sample is suspected of containing a nucleic acid [sequence] which codes for expression of a polypeptide diagnostic for a tumor cell and wherein said compound comprises a polynucleotide complementary to the messenger ribonucleic acid transcribed from a deoxyribonucleic acid [sequence] associated with the production of said polypeptide.

Please add the following new claims:

¹⁴⁸~~146~~. (New) A method of determining the presence or absence of a target nucleic acid in a sample which comprises the steps of

(a) contacting said sample with at least one compound comprising the structure:



wherein each of B, B', B'' represents a purine, deazapurine, or pyrimidine moiety covalently bonded to the C^{1'}-position of the sugar moiety, provided that whenever B, B' or B'' is purine or deazapurine, the sugar moiety is attached at the N⁹-position of the purine or deazapurine, and whenever B, B' or B'' is pyrimidine the sugar moiety is attached at the N¹-position of the pyrimidine;

wherein A represents at least one component of a signalling moiety capable of producing a detectable signal when the compound is incorporated into a double-stranded ribonucleic or deoxyribonucleic acid duplex and comprises at least three carbon atoms;

wherein B and A are attached directly or through a linkage group, said linkage group not interfering substantially with the characteristic ability of B to hybridize with said target or of A to produce a detectable signal;

wherein if B is purine, A is attached to the 8-position thereof, if B is deazapurine, A is attached to the 7-position thereof, and if B is pyrimidine, A is attached to the 5-position thereof;

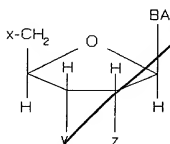
wherein m, n and p are integers, provided that m and p are not simultaneously 0 and provided further n is never 0; and

wherein z represents H- or HO-; and

(b) detecting any signal associated with said compounds hybridized to said target.

147. (New) A method for determining the presence or absence of cells having hormone receptor sites on the surfaces thereof in a sample which is suspected of containing cells having hormone receptor sites on the surfaces thereof, which method comprises the steps of:

(a) contacting said sample with a compound having the structure:



wherein B represents a purine, deazapurine, or pyrimidine moiety covalently bonded to the C1'-position of the sugar moiety, provided that when B is purine or deazapurine, it is attached at the N9-position of the purine or deazapurine, and when B is pyrimidine, it is attached at the N1-position;

wherein A represents at least one component of a signalling moiety and comprises at least three carbon atoms;

wherein B and A are attached together directly or through a linkage group;

wherein if B is purine, A is attached to the 8-position of the purine, if B is deazapurine, A is attached to the 7-position of the deazapurine, and if B is pyrimidine, A is attached to the 5-position of the pyrimidine, and wherein either z is H- or HO- and x and y together form the moiety



or x is HO- and y and z together form the moiety



(b) disrupting said cells to produce cell surface fragments to which said compound is bound;

(c) separately recovering said cell surface fragments;
and

(d) detecting said compound in said fragments so as to identify said hormone receptor sites.

REMARKS

The communication dated July 13, 1992 indicated that the amendments to the claims requested in the Response filed on April 21, 1992 were not made due to the presence of underlining or brackets in the claims that are intended to appear in the printed patent and are properly part of the claimed material. The amendments to the claims made in the present Response are essentially the same as the amendments made in the Response filed on April 21, 1992, except that (a) the new independent claims have been numbered 146 and 147 instead of 145 and 146, due to the presence of a claim numbered 145 when the application